Attorney Docket No. CORR-004/01US **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Ben A. HITT et al.		Examiner:	Clow, Lori A.
Serial No.:	10/628,137	Art Unit:	1631
Filed:	July 28, 2003	Confirmation No.:	4524

For: **QUALITY ASSURANCE/QUALITY CONTROL FOR HIGH-THROUGHPUT BIOASSAY PROCESS**

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SUBMISSION IN RESPONSE TO NOTICE OF NON-COMPLIANT AMENDMENT UNDER 37 CFR 1.121

In Response to the Notice of Non-Compliant Amendment under 37 CFR §1.121 dated March 13, 2007, the period for reply being one-month from such date, the Applicants submit the following documents.

It is not believed that extensions of time are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 CFR §1.136(a), and any fees required therefore (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-1283.

REMARKS

In response to the Office Action mailed on October 4, 2006, the Applicants' representative filed a Reply and Amendment on December 19, 2006. It is respectfully submitted that a *bona fide* attempt to reply to the Office Action mailed on October 4, 2006 was made by the Applicants and/or the Applicants' representative. A Notice of Non-Compliant Amendment under 37 CFR §1.121 was mailed on March 13, 2007. The Notice of Non-Compliant Amendment indicated that the Reply and Amendment did not include a proper status identifier for each of the claims

Accordingly, this submission includes Appendix A, which includes a new "Amendments to the claims" section. The new "Amendments to the claims" section includes a complete listing of the claims along with a proper status identifier for each of the claims.

The Examiner is invited to contact the undersigned to discuss any matter concerning this application.

The Director is hereby authorized to charge any appropriate fees under 37 CFR. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-1283.

Dated: April 11, 2007

Respectfully submitted,
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APPENDIX A

In the Claims:

Please cancel claim 42 (claims 1-27 were previously canceled). Please add claim 55. The following listing of claims will replace all prior versions and listings of claims in the application. Currently amended claims are shown with additions underlined and deletions in ~~strikethrough text~~. No new matter is added by this amendment.

1.-27. (Canceled)

28. (Currently amended) A method of determining whether mass spectral data from a test serum is acceptable for analysis in~~evaluating results from~~ a bioassay ~~biological diagnostic~~ using ~~mass spectral data from~~ biochips, comprising:

selecting a diverse group of sera, the diverse group of sera having different characteristics;

obtaining information associated with a mass spectrum of each of the sera from the diverse group of sera using each of a plurality of control biochips;

generating a control model based at least in part on the spectra obtained from the diverse group of sera, the control model including at least one ~~model~~centroid located in an n-dimensional space defined by n mass spectral features included in the control model;

performing mass spectrometry on a test serum applied to a test biochip to obtain a test spectrum associated with the test serum;

mapping the test spectrum ~~obtained from said performing~~ to the n-dimensional space; and

if it is determined that the test spectrum maps to the n-dimensional space within an acceptable distance from said at least one centroid in the control model, certifying that ~~centroid, submitting~~ the test spectrum is acceptable for analysis in the bioassay ~~to the biological diagnostic~~.

29. (Previously presented) The method of claim 28, further comprising:

classifying a biological state from the test spectrum based on a predetermined biological state model.

30. (Currently amended) The method of claim 28, wherein if the test spectrum does not map to the n-dimensional space within an acceptable distance from said at least one centroid in the control~~the~~ model ~~centroid~~, and the test biochip is a first biochip, the method further comprising:

repeating the steps of performing and mapping for a second biochip different from said test biochip.

31. (Previously presented) The method of claim 28, said selecting further comprising:

selecting at least two different sera from a pool of diverse sera, the pool of diverse sera consisting of: sera from healthy males, sera from healthy females, sera from males afflicted with a disease, sera from females afflicted with a disease, sera from persons of different races, and sera from people of different ages.

32. (Currently amended) The method of claim 28, wherein said generating includes:

identifying at least one cluster in common to the sera of the diverse group of sera and the plurality of different control biochips that contains said at least one centroid in the control model; and

if it is determined that the test spectrum maps to the n-dimensional space within said at least one cluster, certifying that the test spectrum is acceptable for analysis in the bioassay~~selecting only one cluster as the model centroid of the control model~~.

33. (Previously presented) The method of claim 28, wherein the obtaining information includes:

obtaining information on sera applied to at least two types of biochips, the types of biochips being at least two of a cationic exchange biochip, an anionic exchange biochip, and an immobilized metal biochip.

34. (Previously presented) The method of claim 28, wherein the test biochip is one of the plurality of different biochips.

35. (Previously presented) The method of claim 28, wherein the test biochip is not one of the plurality of different biochips.

36. (Currently amended) A method of determining whether mass spectral data from a test serum is acceptable for analysis in a bioassay ~~evaluating results from a biological diagnostic test~~ employing a control model generated based on mass spectra obtained from application of a plurality of different sera to a plurality of different biochips, the control model including at least one ~~model~~ centroid located in an n-dimensional space defined by n mass spectral features included in the model, comprising:

applying a test serum to a spot on a test biochip;

performing mass spectrometry on the test serum to obtain test spectral data associated with the test serum and the test biochip; and

mapping the test spectrum to the n-dimensional space; and

if it is determined that the test spectrum maps to the n-dimensional space within an acceptable distance from said at least one centroid in the control model ~~centroid~~, certifying that~~submitting~~ the test spectrum is acceptable for analysis in~~to~~ the bioassay~~biological diagnostic~~.

37. (Currently amended) The method of claim 36, further comprising:

classifying a biological state from ~~where the submitting includes submitting~~ the test spectrum based on a predetermined ~~to the biological diagnostic to determine if the test serum exhibits a particular~~ biological state model.

38. (Previously presented) The method of claim 36, wherein said performing mass spectrometry includes performing surface enhanced laser desorption/ionization time of flight (SELDI-TOF) mass spectrometry.

39. (Currently amended) The method of claim 36, wherein said ~~biological diagnostic~~ bioassay is ~~a disease model~~ capable of determining if the test serum exhibits a disease state ~~associated with the disease model~~.

40. (Currently amended) A method of determining whether mass spectral data from a test serum is acceptable for analysis in a bioassay~~evaluating results from a biological diagnostic~~ using ~~mass spectral data from the application sera to~~ a biochip, comprising:

providing in an n-dimensional space defined by n mass spectral features a location of at least one ~~model~~ centroid associated with one biochip and that distinguishes the one biochip from at least one second biochip;

generating a test mass spectrum from the application of a test serum to a test biochip;

mapping the test mass spectrum to the n-dimensional space; and

if it is determined that the test mass spectrum maps to the n-dimensional space within an acceptable distance from the at least one~~model~~ centroid, certifying that the test mass spectrum is acceptable for analysis in the bioassay ~~with the biological diagnostic~~.

41. (Currently amended) A method of determining whether mass spectral data from a test sample is acceptable for analysis in~~evaluating results for~~ a bioassay that generates mass spectral data from the application of a sample~~serum~~ to a biochip, comprising:

providing a location in an n-dimensional space defined by n mass spectral features of at least one ~~model~~ centroid in the model associated with a ~~preferred~~ biochip;

receiving mass spectral data associated with the test sample;

providing a location in the n-dimensional space of at least one test centroid associated with the mass spectral data from the~~a~~ test sample;

comparing the at least one test centroid to the at least one ~~model~~ centroid in the model to determine the displacement in the n-dimensional space of the at least one test centroid from the at least one centroid in the model~~centroid~~; and

if it is determined that the displacement is within an acceptable distance, certifying that the mass spectral data from the test sample is acceptable for analysis in the bioassay.

42. (Canceled)

43. (Previously presented) The method of claim 41, wherein the sample is serum.

44. (Previously presented) The method of claim 41, wherein the mass spectral data is generated by surface enhanced laser desorption/ionization time of flight (SELDI-TOF) mass spectrometry.

45. (Currently amended) A method of determining whether mass spectral data from a test sample is acceptable for analysis in ~~evaluating results for~~a bioassay that generates mass spectral data from a sample that is applied to a biochip, comprising:

providing a location in an n-dimensional space defined by n mass spectral features of at least one ~~model~~ centroid in a model associated with a ~~preferred~~ biochip;

receiving mass spectral data associated with the test sample;

providing a location in the n-dimensional space of at least one test centroid associated with the mass spectral data from thea test sample; ~~and~~

comparing the at least one test centroid to the ~~at least one~~ model ~~centroid~~ to determine the displacement in the n-dimensional space of the at least one test centroid from the at least one centroid in the model~~-centroid~~; and~~wherein the magnitude of the displacement is an indicator as to reliability of the bioassay applied to the test sample~~

if it is determined that the magnitude of the displacement is acceptable, certifying that the mass spectral data from the test sample is acceptable for analysis in the bioassay.

46. (Currently amended) The method of claim 45, wherein the test sample is accepted for analysis if the displacement of the at least one test centroid from the at least one ~~model~~ centroid in the model is within an acceptable distance.

47. (Previously presented) The method of claim 45, wherein the sample is serum.

48. (Previously presented) The method of claim 45, wherein the mass spectral data is generated by surface enhanced laser desorption/ionization time of flight (SELDI-TOF) mass spectrometry.

49. (Currently amended) A method of evaluating results for a bioassay that generates mass spectral data from the application of a serum to a biochip, comprising:

selecting a diverse group of sera, the diverse group of sera having different characteristics;

selecting a control biochip of a predetermined type;

obtaining information associated with a mass spectrum of each of the sera from the diverse group of sera using the control biochip;

generating a ~~control~~ model based at least in part on the spectra obtained from the diverse group of sera, the ~~control~~ model including at least one ~~model~~ centroid located in an n-dimensional space defined by n mass spectral features included in the ~~control~~ model;

performing mass spectrometry on a test serum applied to a test biochip to obtain a test spectrum associated with the test serum;

mapping the test spectrum obtained from said performing to the n-dimensional space; and

if the test spectrum maps to the n-dimensional space within an acceptable distance from the at least one ~~model~~ centroid in the model, certifying that the test biochip is acceptable for use in the bioassay.

50. (Currently amended) The method of claim 49, wherein the control biochip is selected from the group consisting~~one~~ of a cationic exchange biochip, an anionic exchange biochip~~,~~ and an immobilized metal biochip.

51. (Currently amended) A method of evaluating results for a biological diagnostic test employing a ~~control~~ model generated based on mass spectra obtained from application of a plurality of different sera to a preferred biochip, the ~~control~~ model including at least one ~~model~~ centroid located in an n-dimensional space defined by n mass spectral features included in the model, comprising:

applying a test serum to a spot on a test biochip;

performing mass spectrometry on the test serum to obtain test spectral data associated with the test serum and the test biochip; and

mapping the test spectrum to the n-dimensional space; and

if the test spectrum maps to the n-dimensional space within an acceptable distance from the at least one ~~model~~ centroid in the model, certifying that the test biochip is acceptable for use in the biological diagnostic test.

52. (Currently amended) The method of claim 51, wherein the certifying includes ~~submitting~~evaluating the test spectrum ~~to the~~in the biological diagnostic test to determine if the test serum exhibits a particular biological state.

53. (Previously presented) The method of claim 51, wherein said performing mass spectrometry includes performing surface enhanced laser desorption/ionization time of flight (SELDI-TOF) mass spectrometry.

54. (Currently amended) The method of claim 51, wherein said biological diagnostic test is a disease model capable of determining if the test serum exhibits a disease state associated with the disease model.

55. (New) The method of claim 41, wherein the biochip is selected from the group consisting of a cationic exchange biochip, an anionic exchange biochip and an immobilized metal biochip.